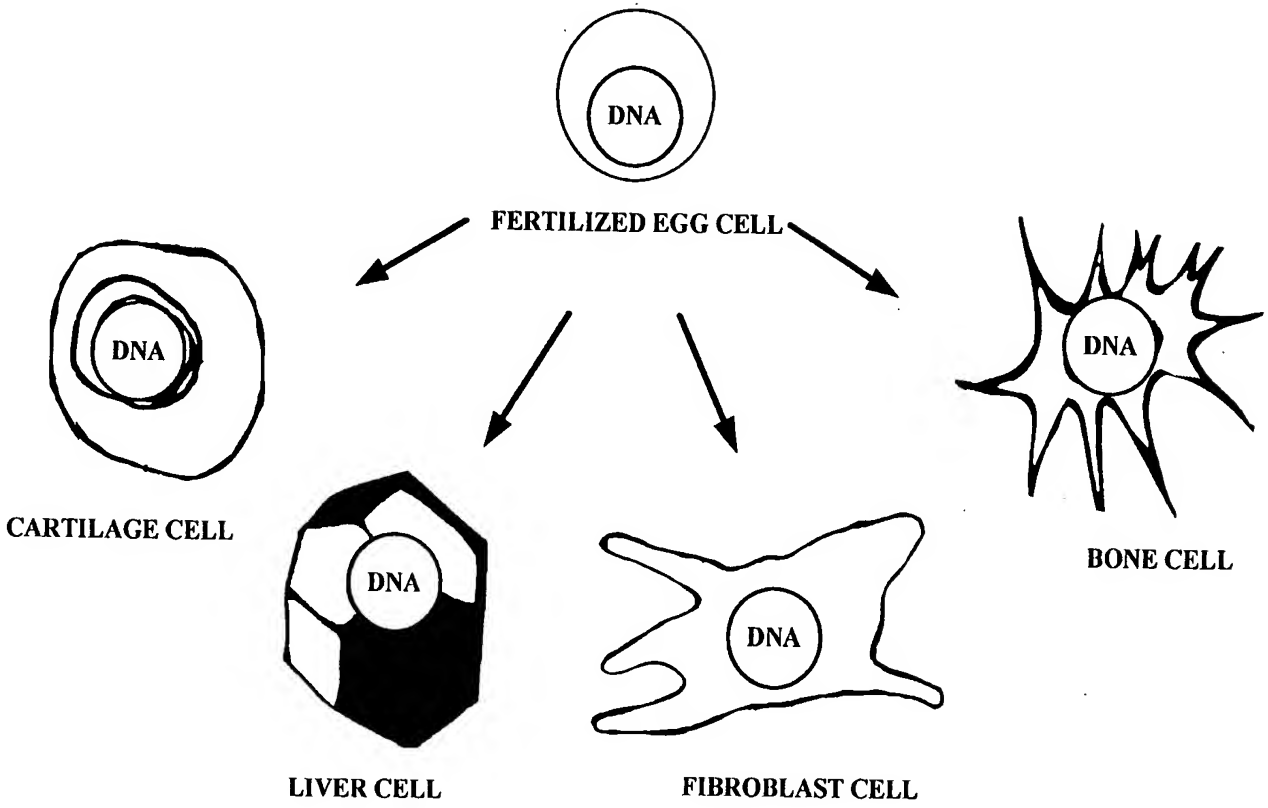
FIG. 1



BEST AVAILABLE COPY

FIG. 2A

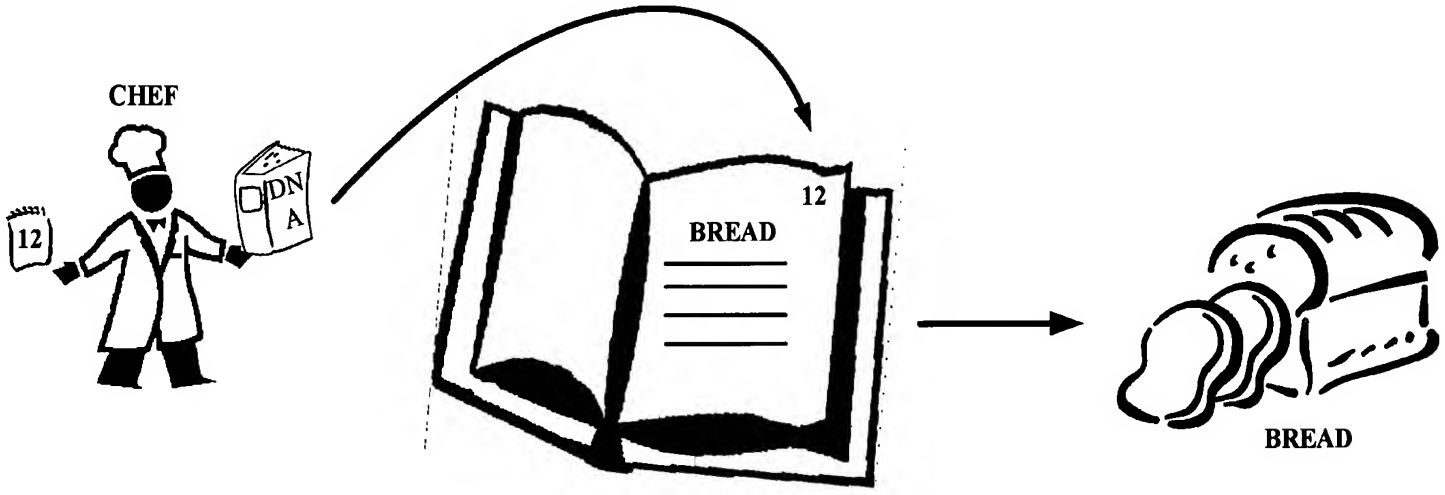


FIG. 2B

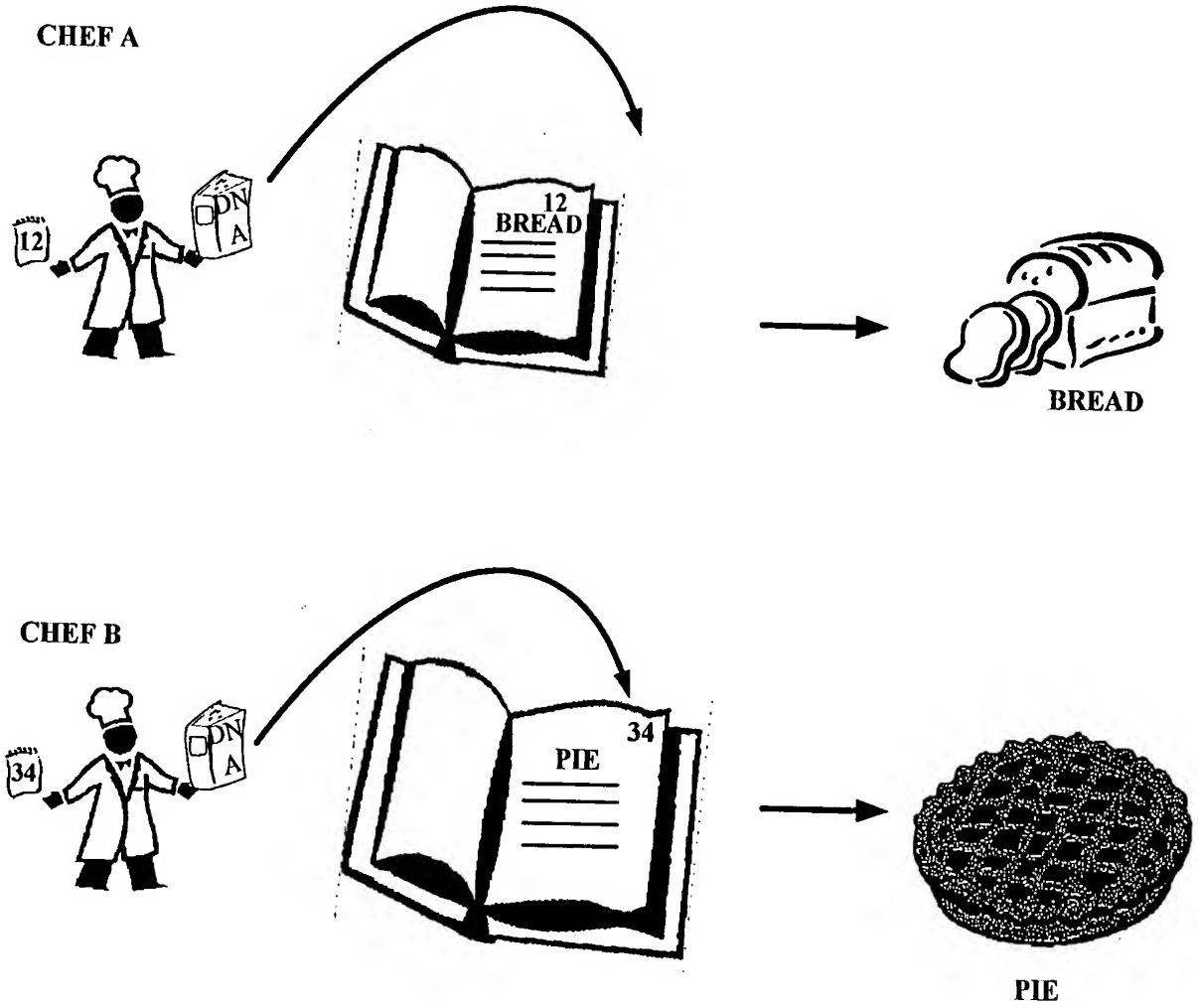


FIG. 3

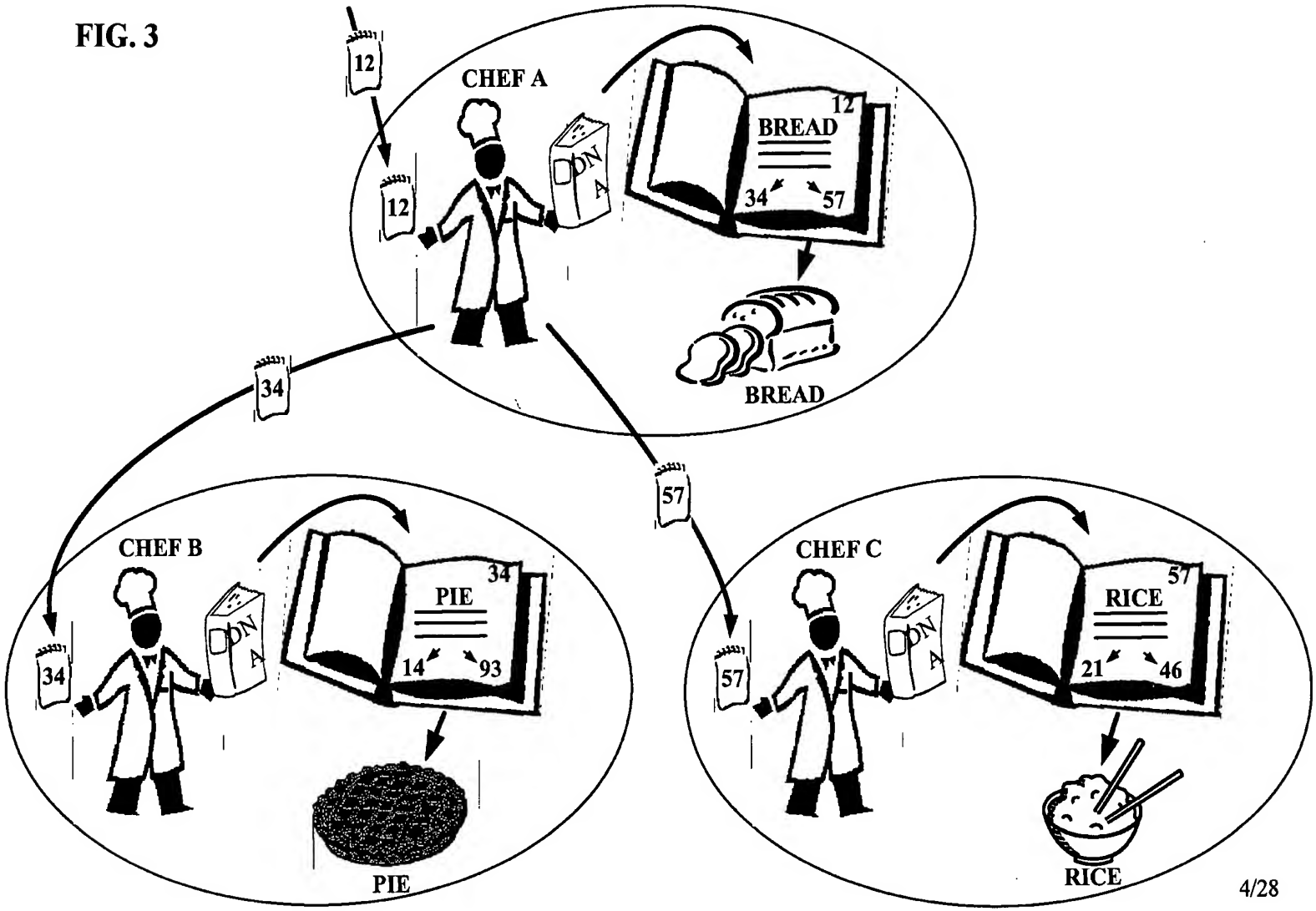

12
CHEF A
12
BREAD
12
34
57
BREAD
34
57
CHEF B
34
PIE
34
14
93
PIE
CHEF C
57
RICE
57
21
46
RICE

FIG. 4

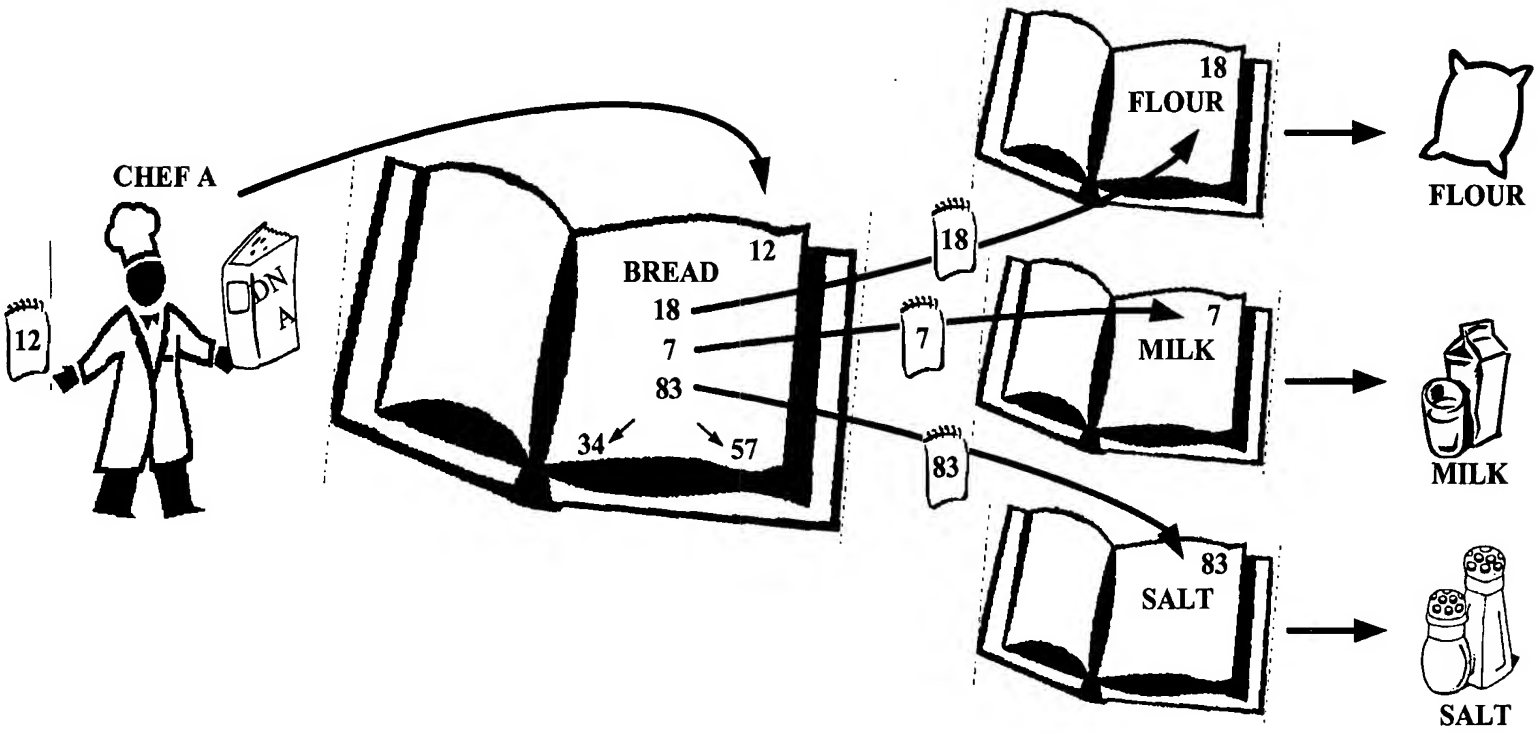

CHEF A
12
DNA
BREAD
12
18
7
83
34
57
18
7
83
18
FLOUR
7
MILK
83
SALT
FLOUR
MILK
SALT

FIG. 5A

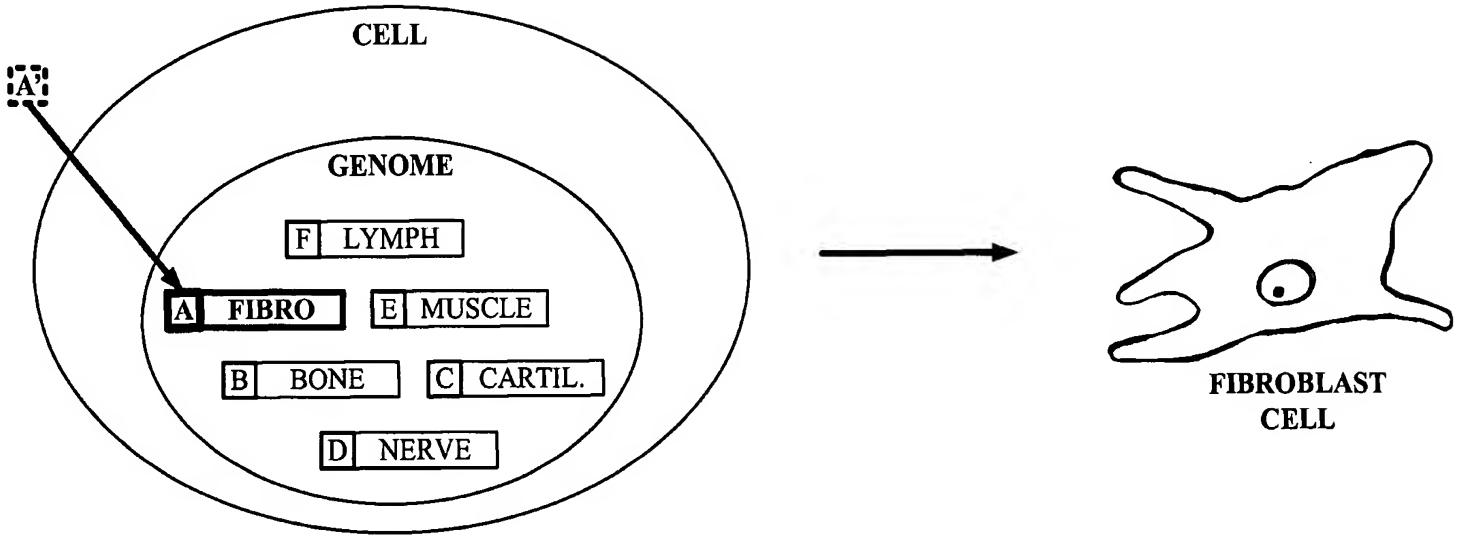

CELL
A'
GENOME
F LYMPH
A FIBRO
E MUSCLE
B BONE
C CARTIL.
D NERVE
FIBROBLAST
CELL

FIG. 5B

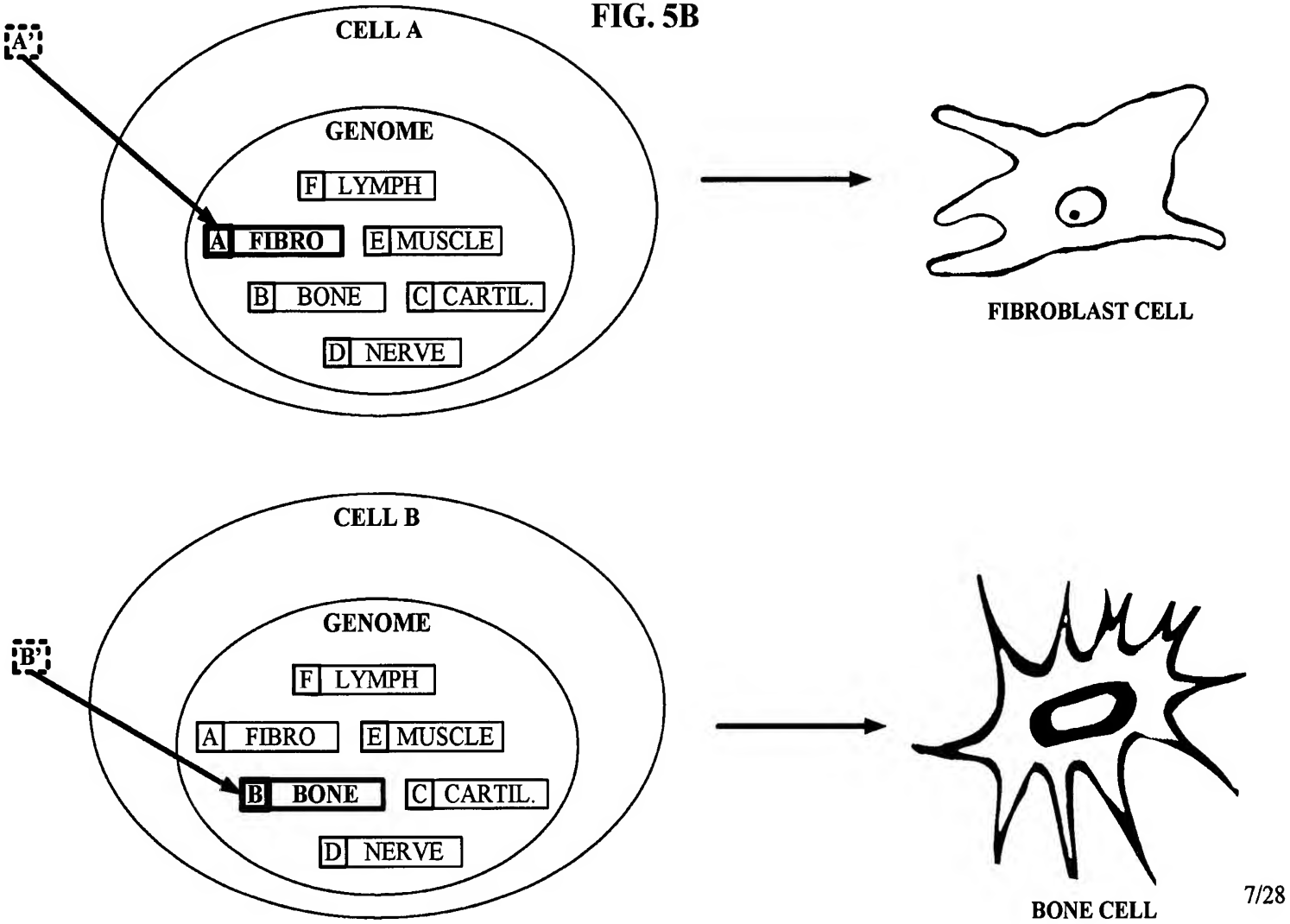

A'
CELL A
GENOME
F LYMPH
A FIBRO
E MUSCLE
B BONE
C CARTIL.
D NERVE
FIBROBLAST CELL
B'
CELL B
GENOME
F LYMPH
A FIBRO
E MUSCLE
B BONE
C CARTIL.
D NERVE
BONE CELL

FIG. 6

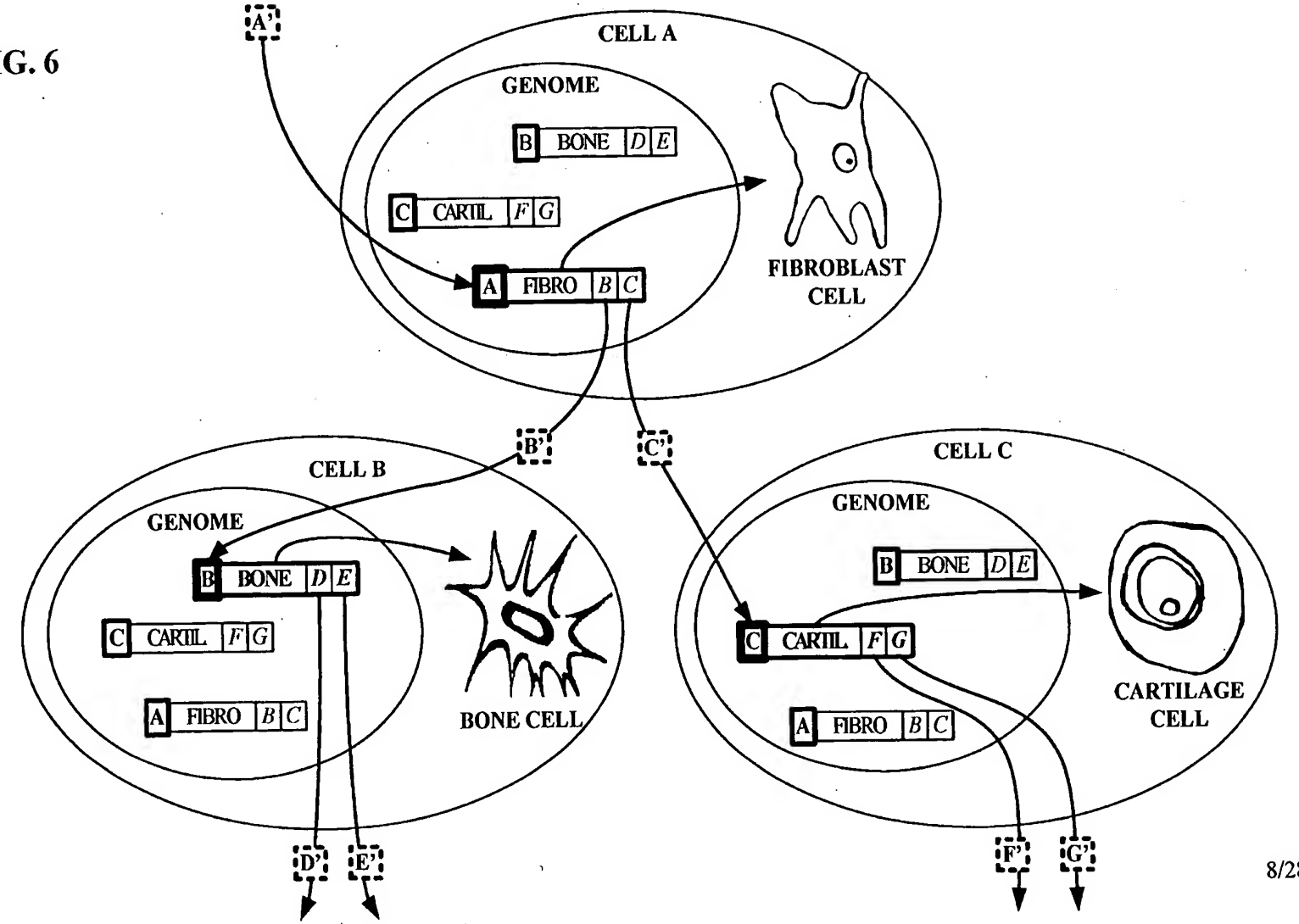

A'
CELL A
GENOME
B BONE D E
C CARTIL F G
A FIBRO B C
FIBROBLAST CELL
B'
C'
CELL B
GENOME
B BONE D E
C CARTIL F G
A FIBRO B C
BONE CELL
CELL C
GENOME
B BONE D E
C CARTIL F G
A FIBRO B C
CARTILAGE CELL
D'
E'
F'
G'

FIG. 7

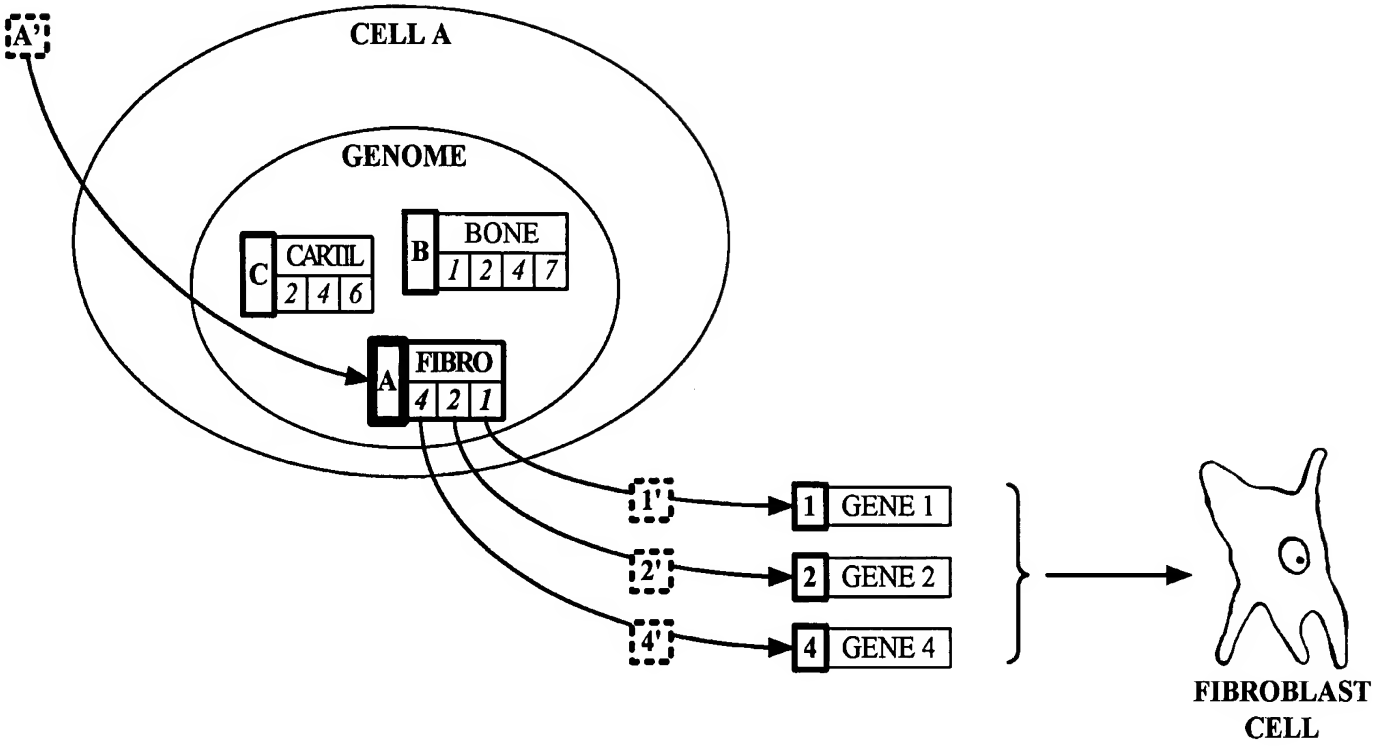

A'
CELL A
GENOME
C
CARTIL
2 4 6
B
BONE
1 2 4 7
A
FIBRO
4 2 1
1'
2'
4'
1 GENE 1
2 GENE 2
4 GENE 4
FIBROBLAST CELL

FIG. 8

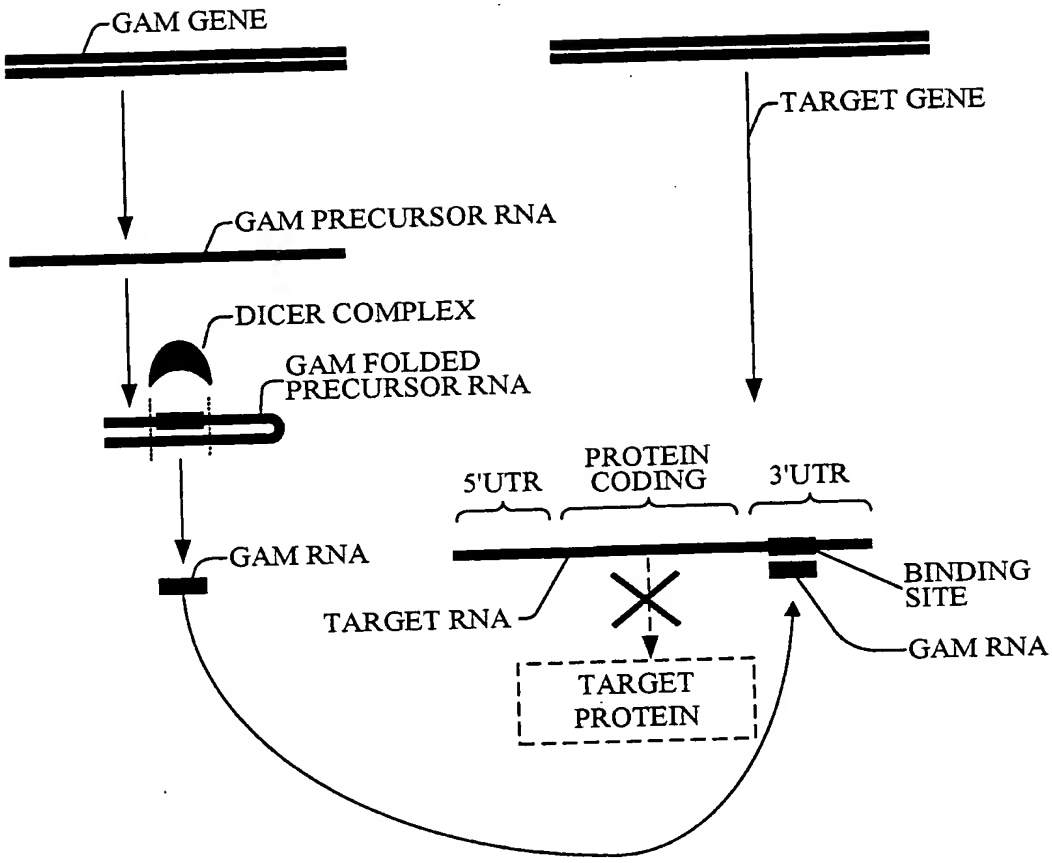

GAM GENE
TARGET GENE
GAM PRECURSOR RNA
DICER COMPLEX
GAM FOLDED PRECURSOR RNA
5'UTR
PROTEIN CODING
3'UTR
GAM RNA
BINDING SITE
TARGET RNA
GAM RNA
TARGET PROTEIN

FIG. 9

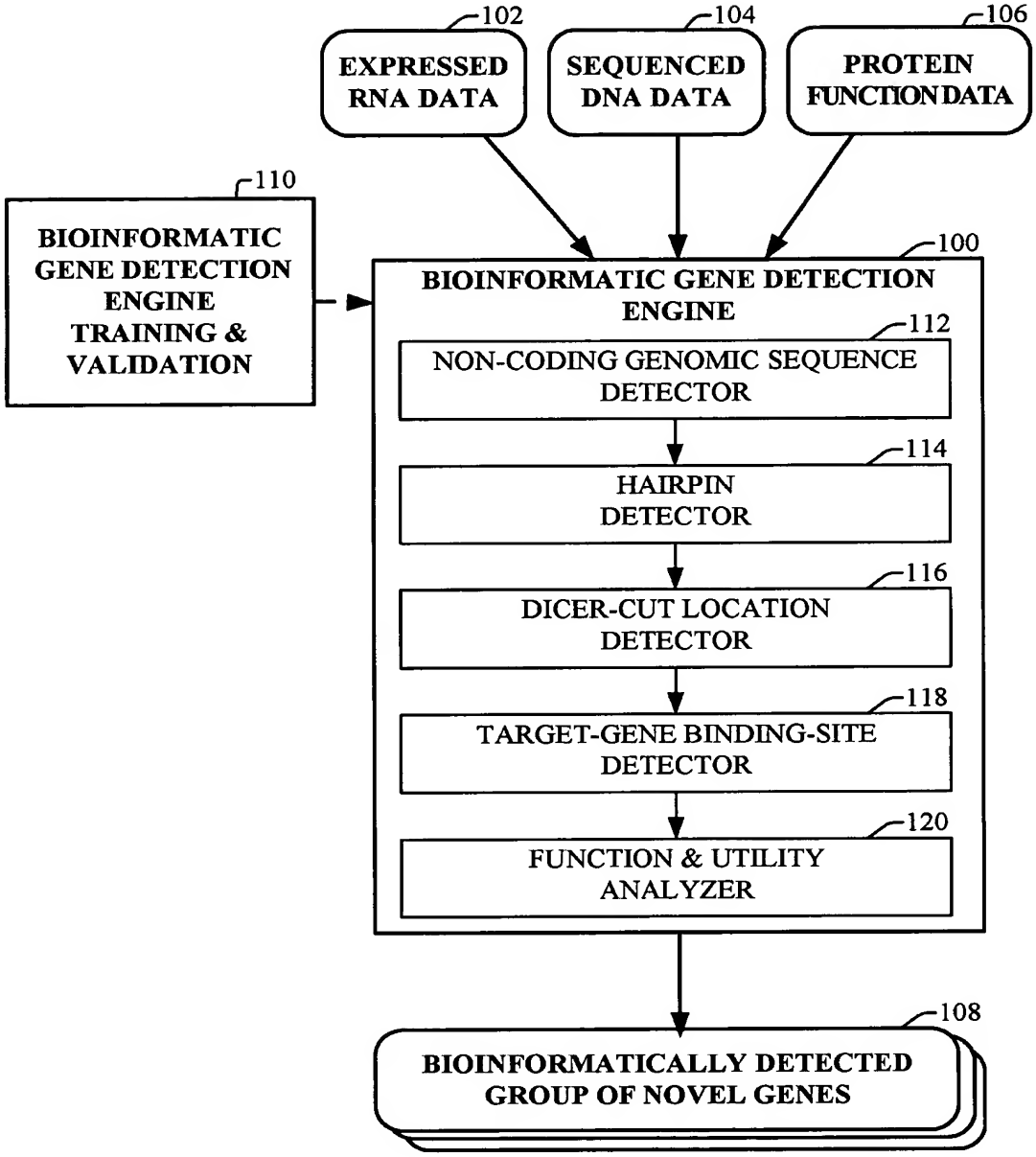

102
EXPRESSED RNA DATA
104
SEQUENCED DNA DATA
106
PROTEIN FUNCTION DATA
110
BIOINFORMATIC GENE DETECTION ENGINE TRAINING & VALIDATION
100
BIOINFORMATIC GENE DETECTION ENGINE
112
NON-CODING GENOMIC SEQUENCE DETECTOR
114
HAIRPIN DETECTOR
116
DICER-CUT LOCATION DETECTOR
118
TARGET-GENE BINDING-SITE DETECTOR
120
FUNCTION & UTILITY ANALYZER
108
BIOINFORMATICALLY DETECTED GROUP OF NOVEL GENES

FIG. 10

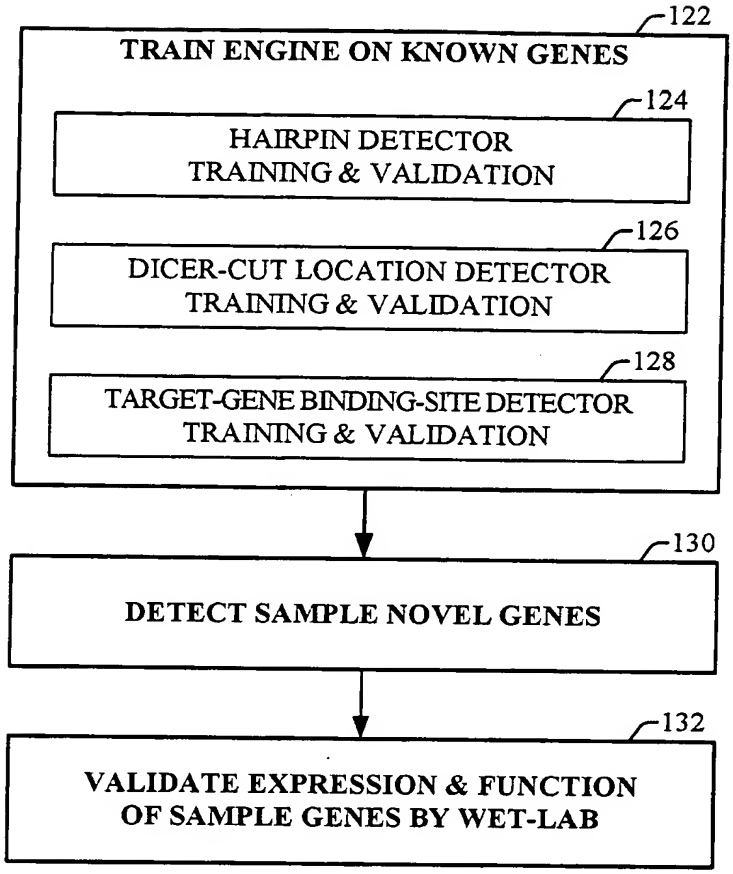

122
TRAIN ENGINE ON KNOWN GENES
124
HAIRPIN DETECTOR
TRAINING & VALIDATION
126
DICER-CUT LOCATION DETECTOR
TRAINING & VALIDATION
128
TARGET-GENE BINDING-SITE DETECTOR
TRAINING & VALIDATION
130
DETECT SAMPLE NOVEL GENES
132
VALIDATE EXPRESSION & FUNCTION
OF SAMPLE GENES BY WET-LAB

FIG. 11A

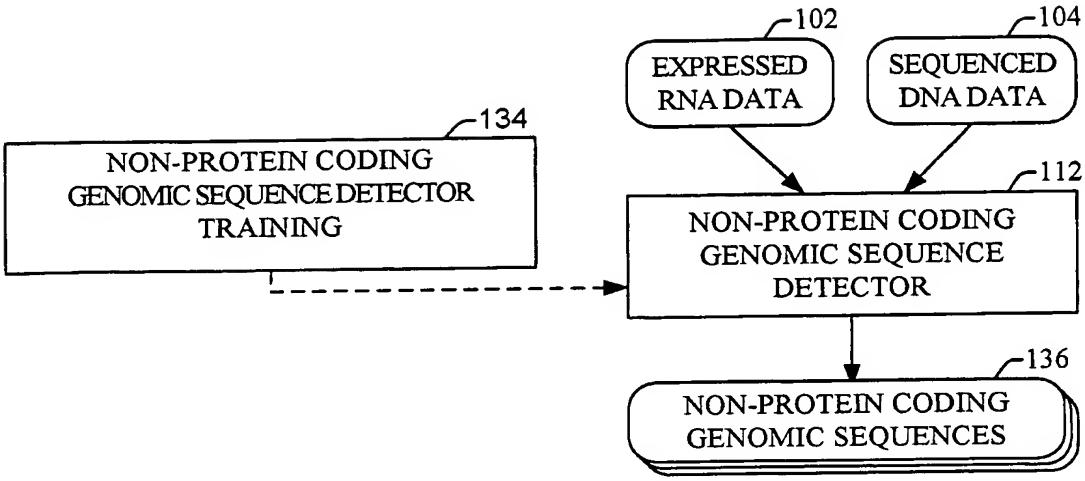


FIG. 11B

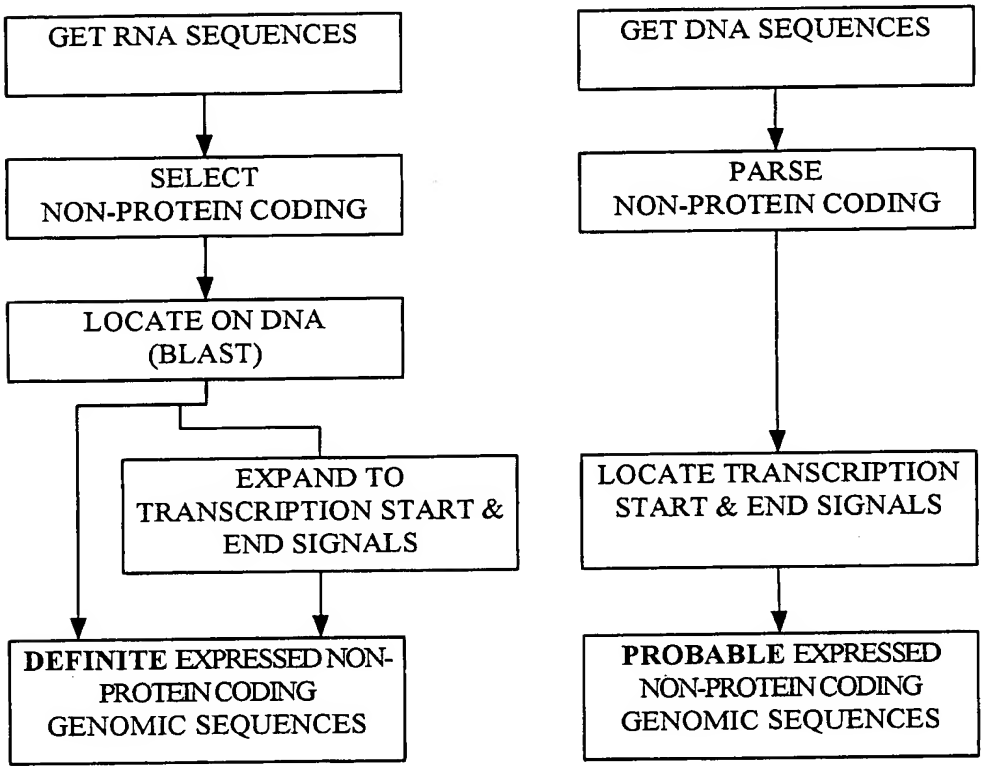


FIG. 12A

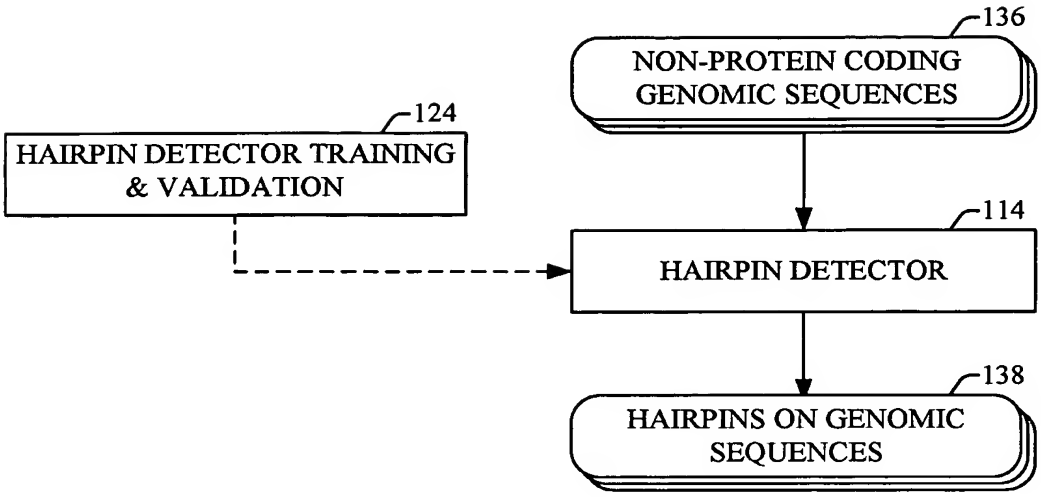


FIG. 12B

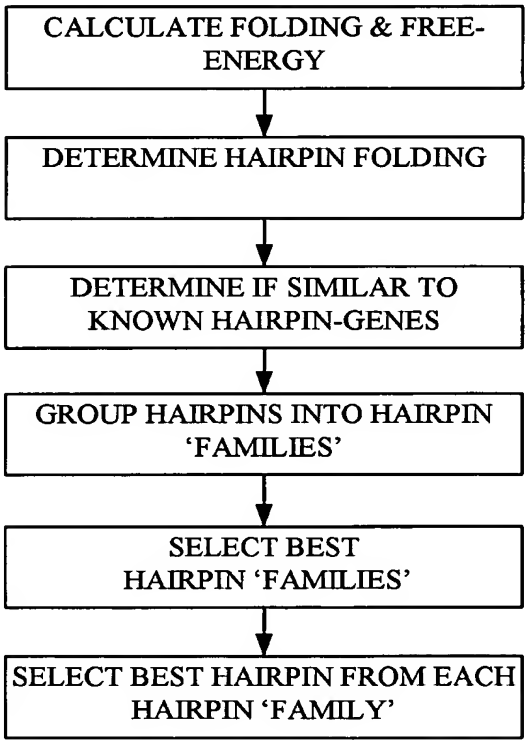


FIG. 13A

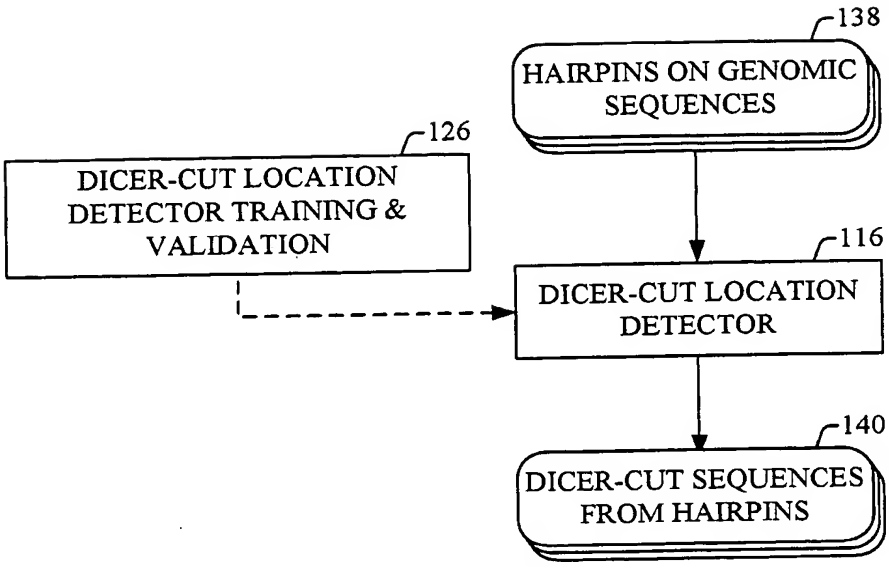

138
HAIRPINS ON GENOMIC SEQUENCES
126
DICER-CUT LOCATION DETECTOR TRAINING & VALIDATION
116
DICER-CUT LOCATION DETECTOR
140
DICER-CUT SEQUENCES FROM HAIRPINS

FIG. 13B

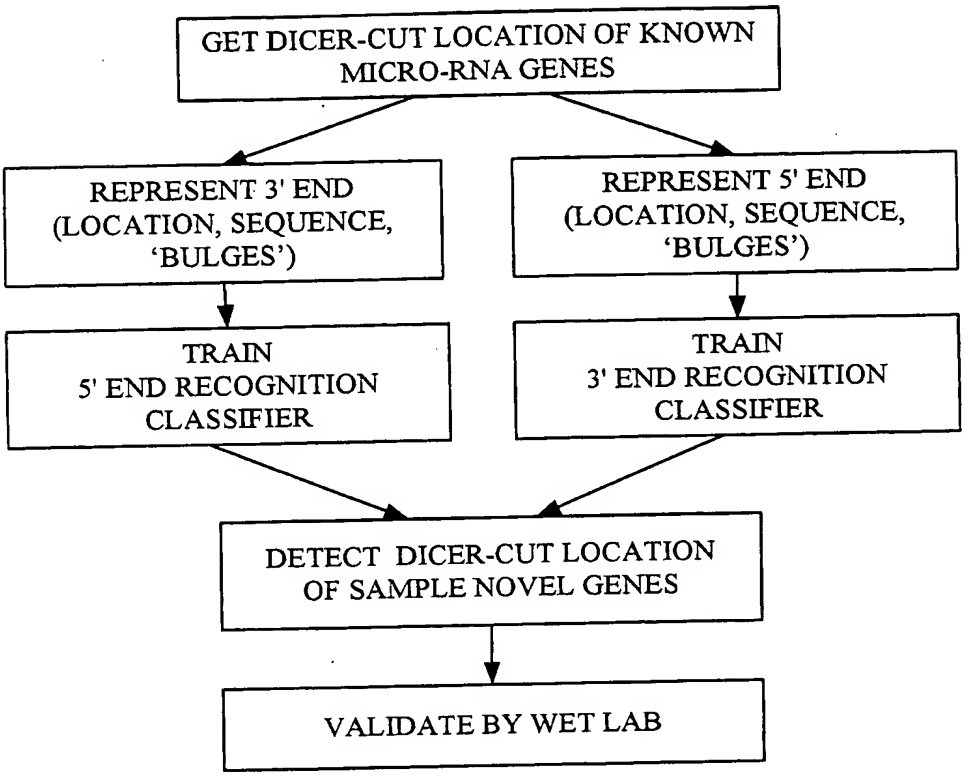

GET DICER-CUT LOCATION OF KNOWN MICRO-RNA GENES
REPRESENT 3' END (LOCATION, SEQUENCE, 'BULGES')
REPRESENT 5' END (LOCATION, SEQUENCE, 'BULGES')
TRAIN 5' END RECOGNITION CLASSIFIER
TRAIN 3' END RECOGNITION CLASSIFIER
DETECT DICER-CUT LOCATION OF SAMPLE NOVEL GENES
VALIDATE BY WET LAB

FIG. 13C

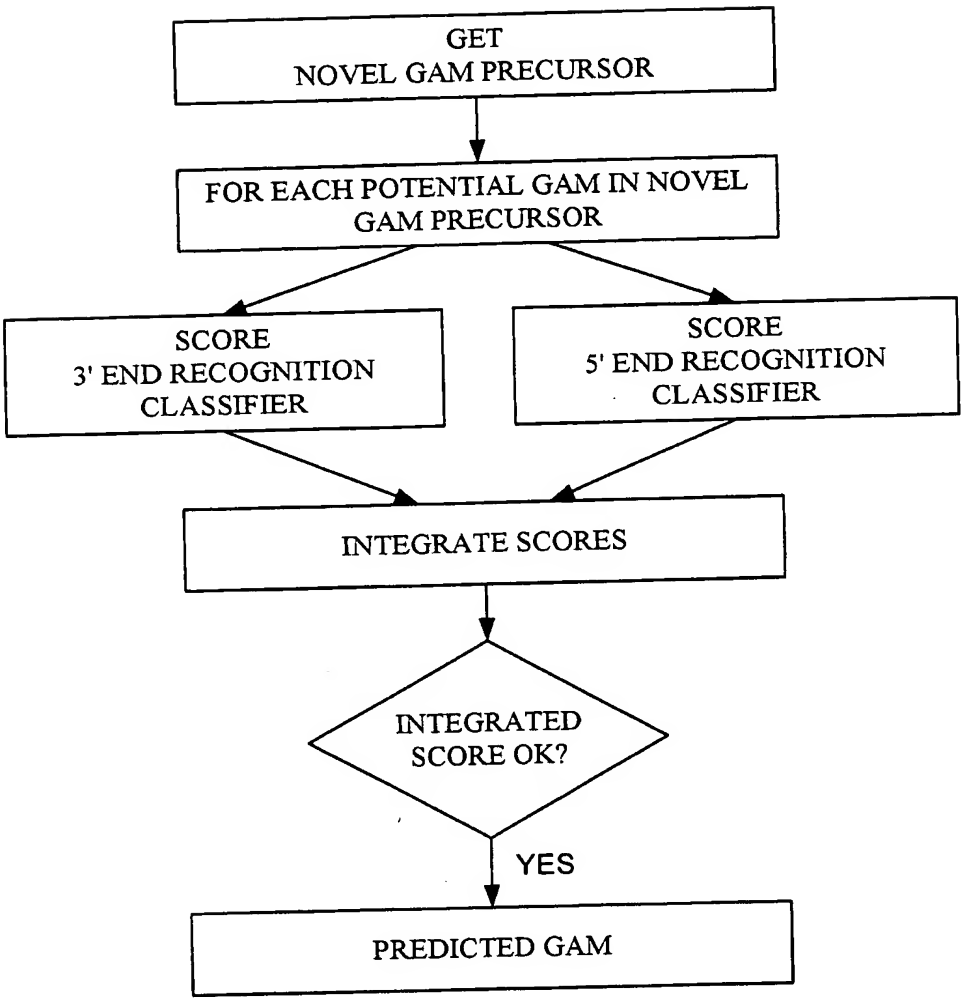

GET
NOVEL GAM PRECURSOR
FOR EACH POTENTIAL GAM IN NOVEL GAM PRECURSOR
SCORE
3' END RECOGNITION
CLASSIFIER
SCORE
5' END RECOGNITION
CLASSIFIER
INTEGRATE SCORES
INTEGRATED
SCORE OK?
YES
PREDICTED GAM

FIG. 14A

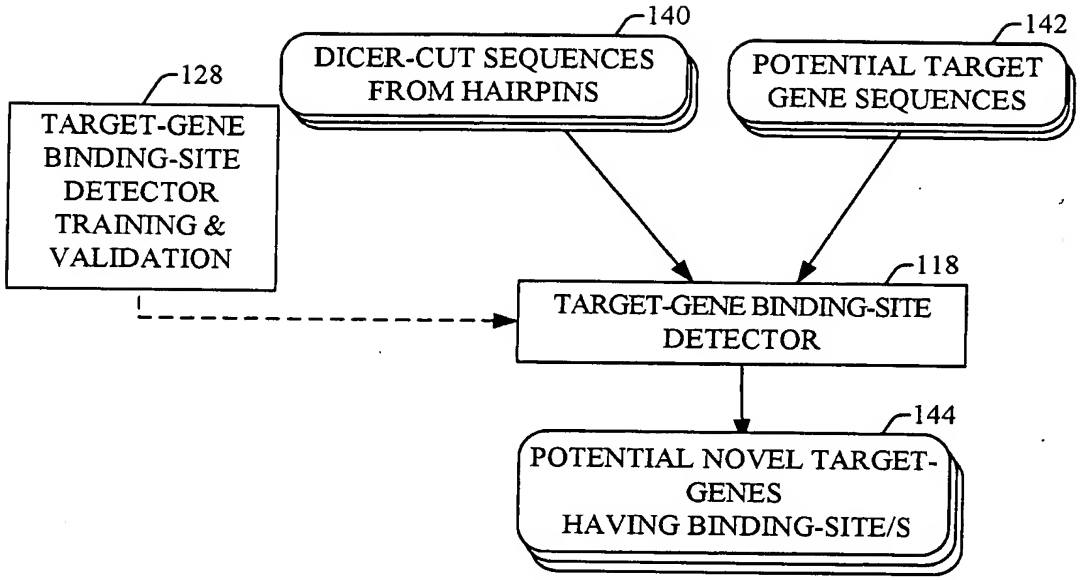


FIG. 14B

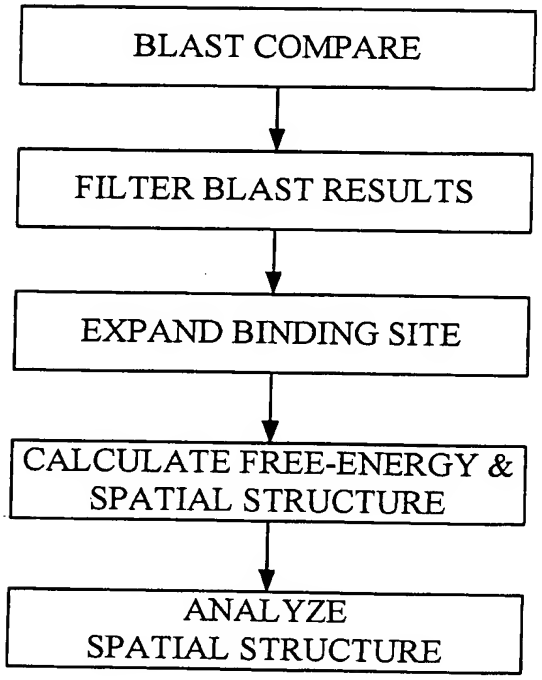


FIG. 15

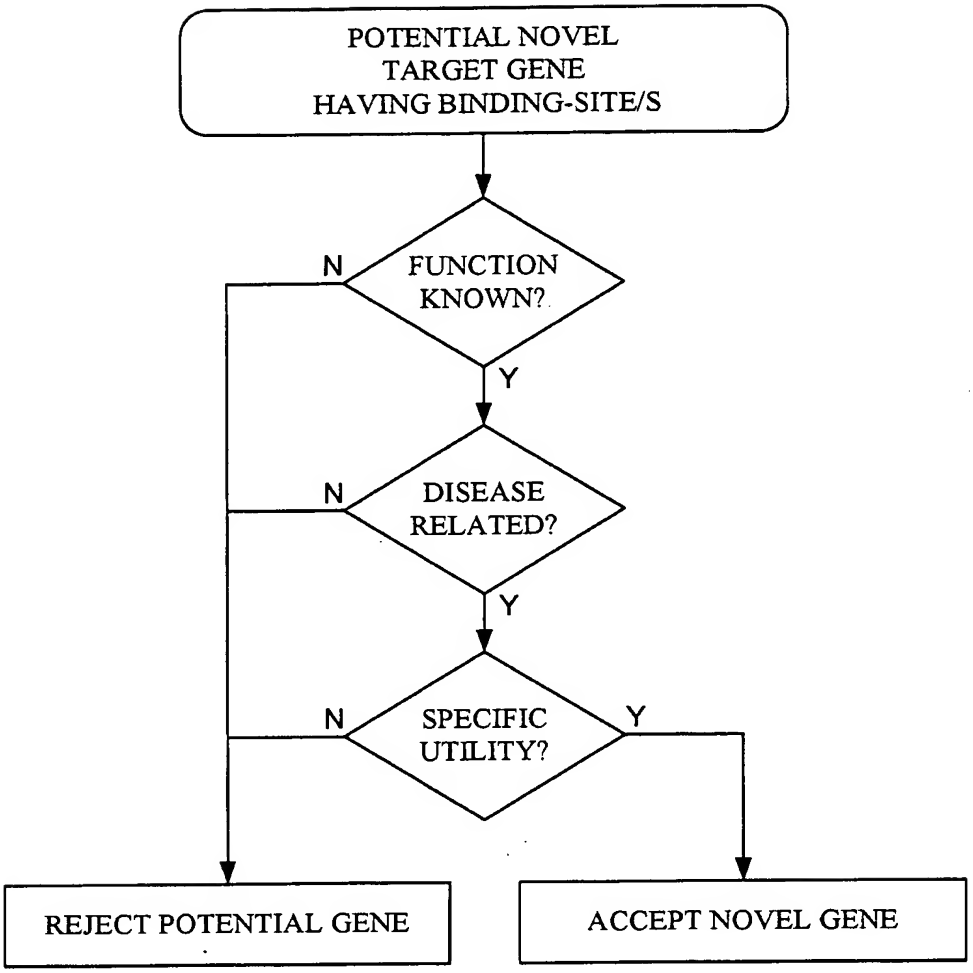

POTENTIAL NOVEL TARGET GENE HAVING BINDING-SITE/S
FUNCTION KNOWN?
N
Y
DISEASE RELATED?
N
Y
SPECIFIC UTILITY?
N
Y
REJECT POTENTIAL GENE
ACCEPT NOVEL GENE

FIG. 16

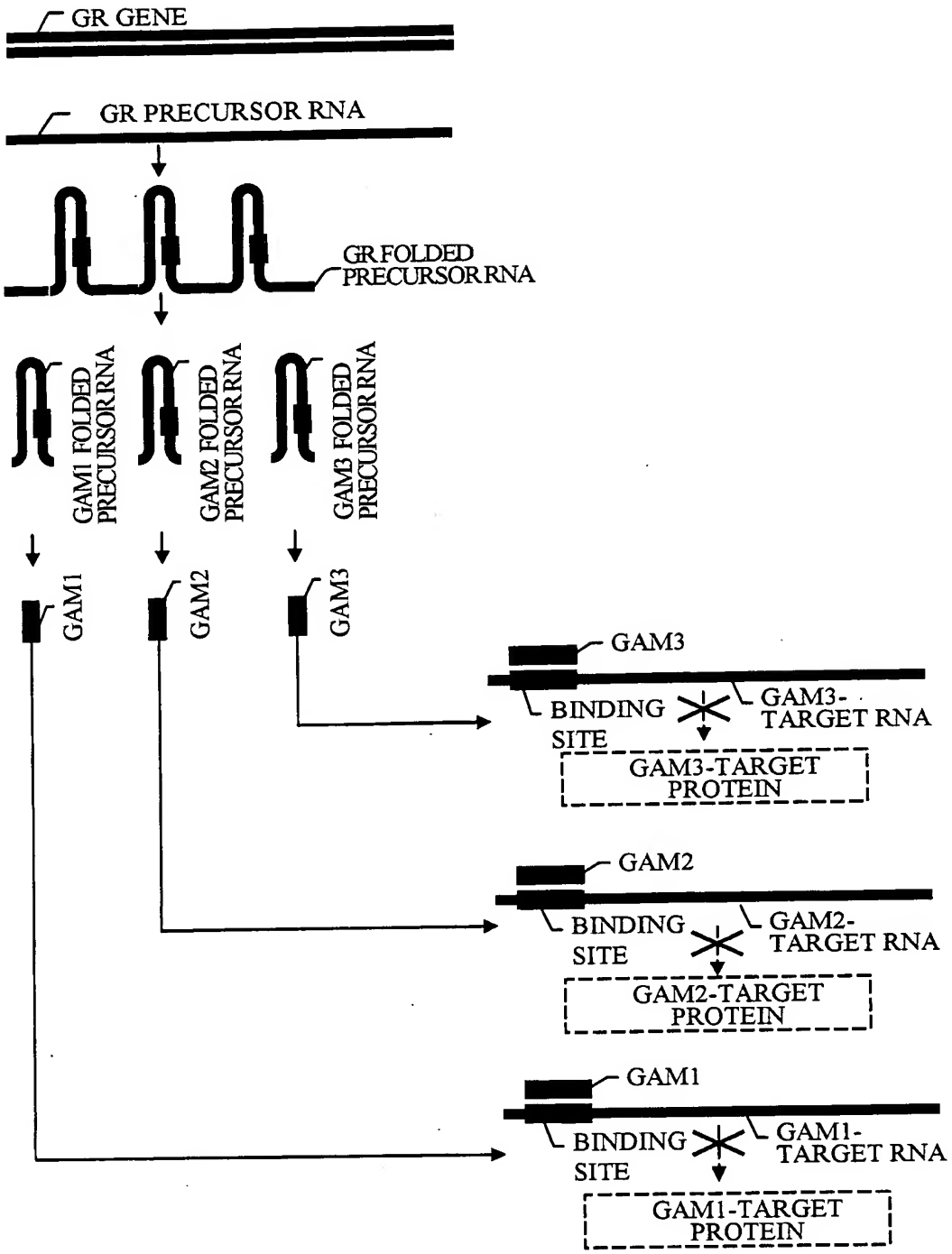

GR GENE
GR PRECURSOR RNA
GR FOLDED PRECURSOR RNA
GAM1 FOLDED PRECURSOR RNA
GAM2 FOLDED PRECURSOR RNA
GAM3 FOLDED PRECURSOR RNA
GAM1
GAM2
GAM3
GAM3
BINDING SITE
GAM3-TARGET RNA
GAM3-TARGET PROTEIN
GAM2
BINDING SITE
GAM2-TARGET RNA
GAM2-TARGET PROTEIN
GAM1
BINDING SITE
GAM1-TARGET RNA
GAM1-TARGET PROTEIN

FIG. 17

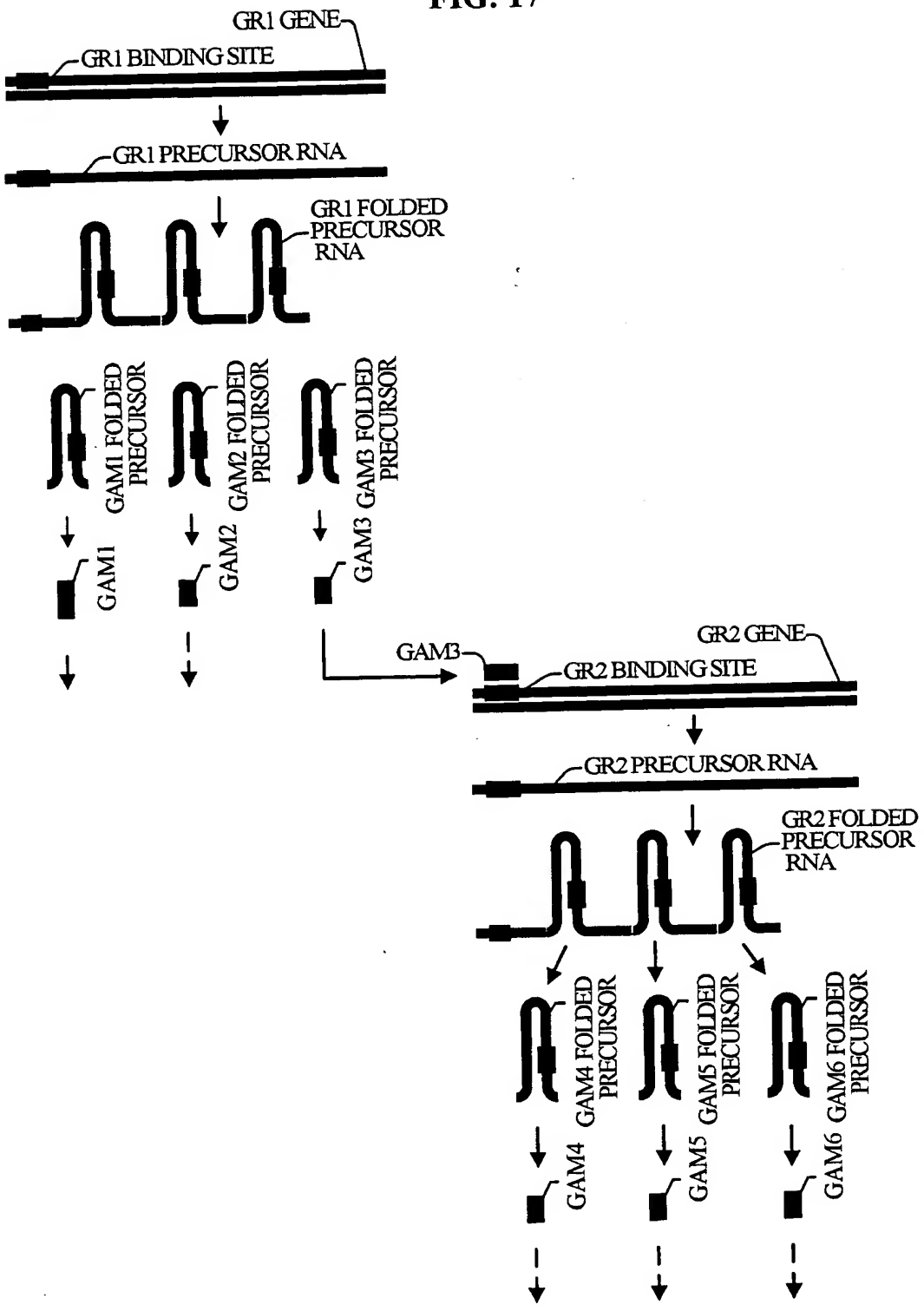

GR1 GENE
GR1 BINDING SITE
GR1 PRECURSOR RNA
GR1 FOLDED PRECURSOR RNA
GAM1 FOLDED PRECURSOR
GAM2 FOLDED PRECURSOR
GAM3 FOLDED PRECURSOR
GAM1
GAM2
GAM3
GAM3
GR2 GENE
GR2 BINDING SITE
GR2 PRECURSOR RNA
GR2 FOLDED PRECURSOR RNA
GAM4 FOLDED PRECURSOR
GAM5 FOLDED PRECURSOR
GAM6 FOLDED PRECURSOR
GAM4
GAM5
GAM6

FIG. 18

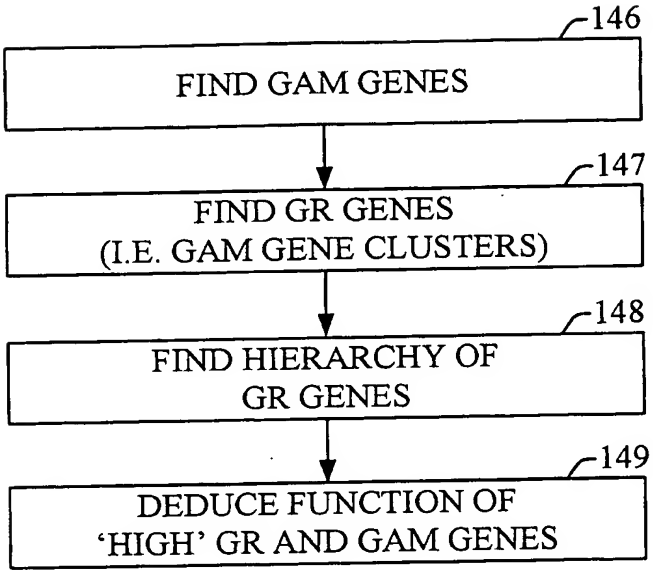

146
FIND GAM GENES
147
FIND GR GENES
(I.E. GAM GENE CLUSTERS)
148
FIND HIERARCHY OF
GR GENES
149
DEDUCE FUNCTION OF
'HIGH' GR AND GAM GENES

FIG. 19

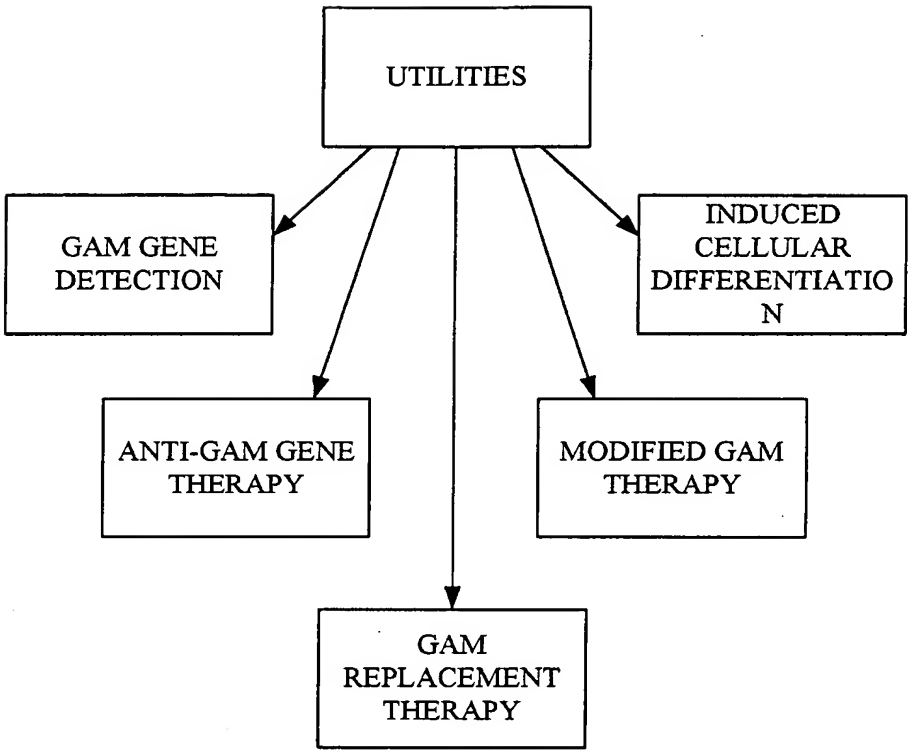

UTILITIES
GAM GENE DETECTION
INDUCED CELLULAR DIFFERENTIATIO N
ANTI-GAM GENE THERAPY
MODIFIED GAM THERAPY
GAM REPLACEMENT THERAPY

FIG. 20A

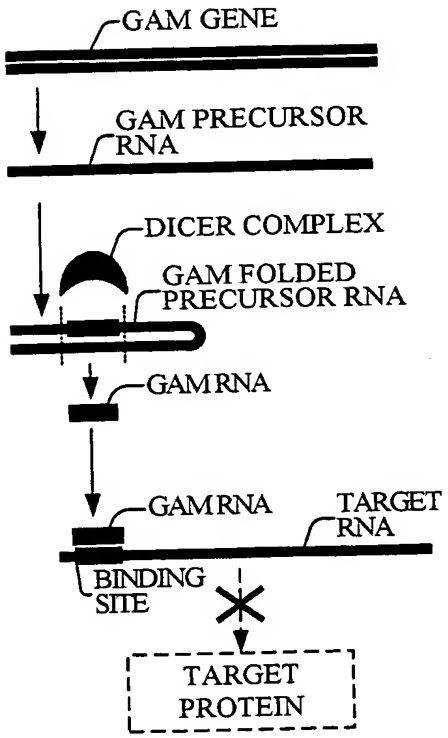
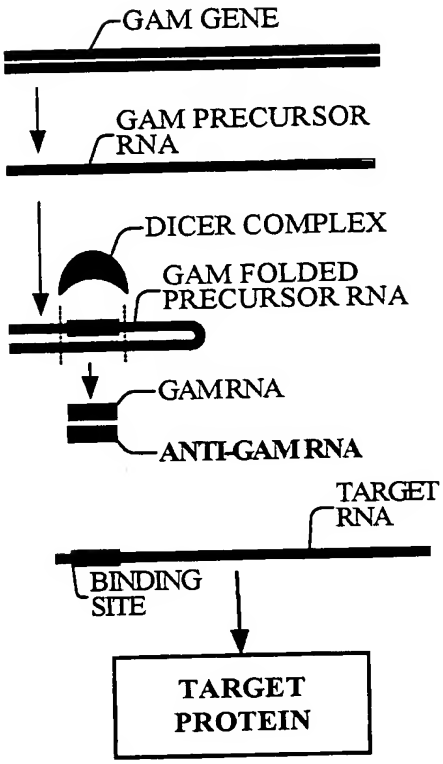


FIG. 20B

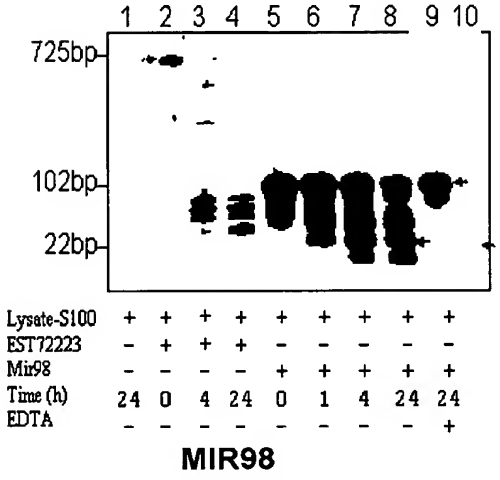


EST72223 sequence:

FIG. 21A

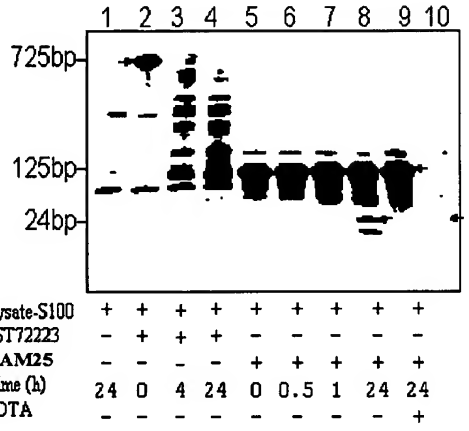
CCCTTATTAGAGGATTCTGCTCATGCCAGGGTGAGGTAGTAAGTTGTATTG
TTGTGGGGTAGGGATATTAGGCCCCAATTAGAAGATAACTATACAACT **MIR98**
TACTACTTTCCCTGGTGTGTGGCATATTCACACTTAGTCTTAGCAGTGTTGCC
TCCATCAGACAAAGTTGTAGATGTTCCTTGGATAATTTGGACTGGAAGAAAAGA
GACATGGAAGGGGACAGATGGTGTTTAGGGTGAGGCAGATGTCATTATAAAGT
GACTTGTCTTTCATTAATTGGAGCATATAATTATTTTACCTTTGGGCATGAACTC
ATTTTGCTATTCTTCAACTGTGTAATGATTGCATTTTATTAGTAATAGAACAGGA
ATGTGTGCAAGGGAATGGAAAGCATACTTTAAGAATTTTGGGCCAGGCGCGGT
GGTTCATGCCTGTAATCCCAGCATTTTTGGGAGGCCGAGGCGGGTGGATCAC
CTGAGGTCAGGAGTTCGAGACCAACCTGGCCAACACGGCGAAACCCCGCCTC
TACTCAAATACAAAAATTAGCCAGGCTTGGTGACACTCGCCTGTGGTCCCAGC
TACTCAGGAGGCT**GAGGCAGGAG**AATTGCTTGAACCCAGGAAGTGGAG **GAM2**
GCTTCAGTGAGCTGAGAACACGCCACTGCACTCCAGTCCTGGGCAAC **5**
AGAGCAAGACTCTGTCTCAGGAAAAAAAAAG

FIG. 21B



MIR98

FIG. 21C



GAM25

FIG. 21D

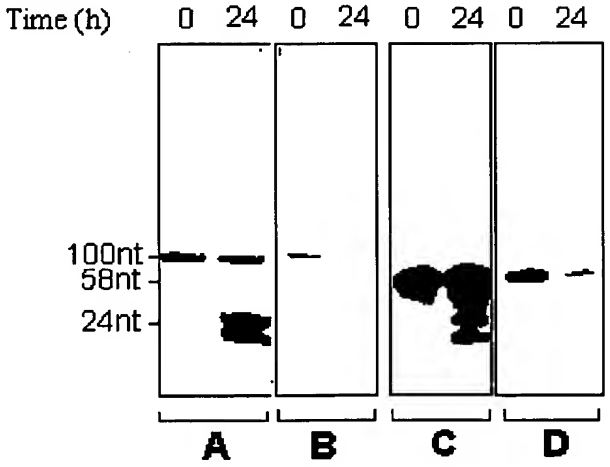
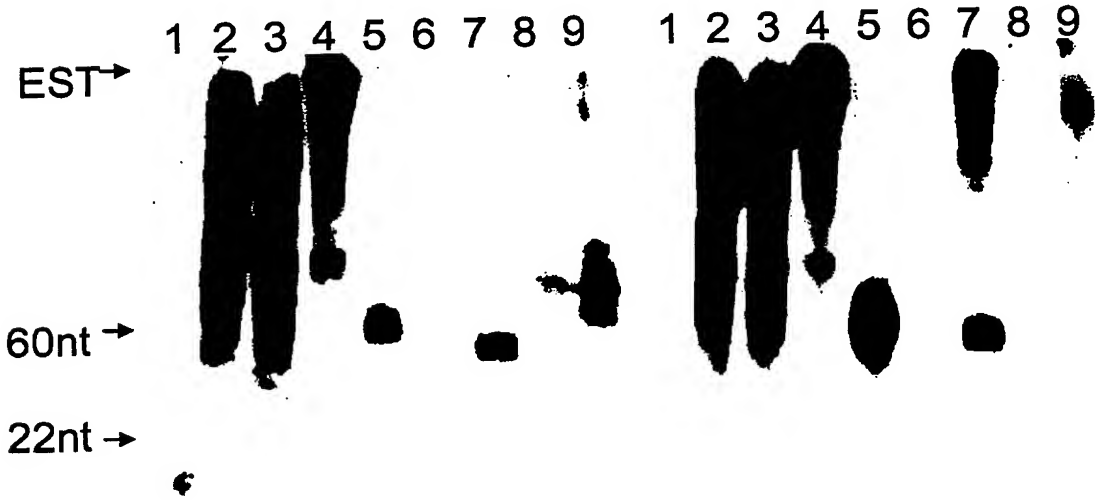


FIG. 22A

dbEST Id. 7929020 (Image4514344) sequence:

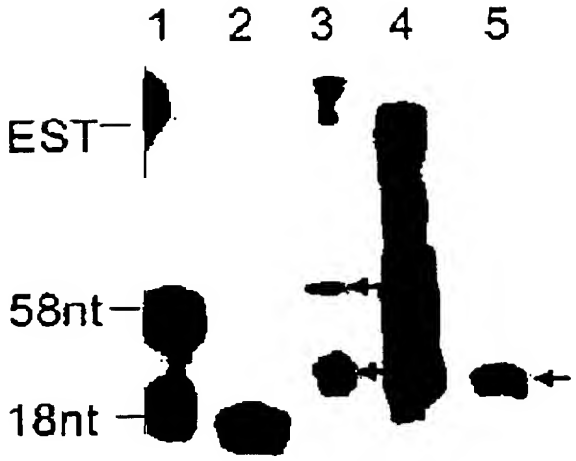
GCAAAAACTGGAAGCATTCCCTTTGAAAACTGGCACAAGACAGGGATGCCCTCTCTCAC
CGCTCCTATTCAACATAGTGTTGGAAGTTCTGGCCAGGGCAATTAGGCAGGAGAAGGAA
ATAAAGGGTATTCAATTAGGAAAAGAGCAAGTCAAATTGTTCCTGTTTGCAGATGACAT
GATTGTATATCTAGAAAACCCCATTGTCTCAGCCCCAAATCTCCTTAAGCTGATAAGCA
ACTTCAGCAAAGTCTCAGGATACAAAATAAATGTACAAAAATCACAAGCATTCTTACAC
ACCAACAACAGAAAAACAGAGCCAAATCATGAGTGAACTCCCATTCACAATTGCTTCAA
AGAGAATAAAATACCTAGGAATCCAACTTACAAGGGATGTGAAGGACCTCTTCAAGGAG
AACTACAAACCACTGCTCAAGGAAATAAAAGAGGATACAAACAAATGGAAGAACATTCC
ATGCTCATGGGTAGGAAGAATCAATATTGTGAAAATGGCCATACTGCCCAAGGTAATTT
ACAGATTCAATGCCATCCCCATCAAGCTACCAATGACTTTCTTCACAGAATTGGAAAAA
ACTACTTTAAAGTTCATATGGAACCAAAAAAGAGCCCGCATCGCCAAGTCAATCCTAAG
CCAAAAGAACAAAGCTGGAGGCATCACACTACCTGACTTCAAACTTTACTACAAGGCTA GAM
CAGTAACCAAAACAGCATGGTACTGGTACCAAAACAGAGATATAGATCAATGGAACAGA 24
ACAGAGCCCTCAGAAATAACGCCGAATACCTACAACTATCTGATCTTTGACAAACCTGA
GAAAAACAAGCAATGGGGAAAGGATTCCCTATTTAATAAATGGTGCTGGGAAAACTGAC
TAGCCATATGTAGAAAGCTGAAACTGGATCCCTTCCTTACACCTTATACAAAAATCAAT
TCAAGATGGATTAAAGATTTAAACGTTAGACCTAAAACCATAAAAACCCTAGAAGAAAA
CCTAGGCATTACCATTCAGGACATAGGCATGGGCAAGGACTTCATGTCCAAAACACCAA
AAGCAATGGCAACAAAAGACAAAATTGACAAATGGGATCTAATTAAACTAAAGAGCTTC
TGCACAGCAAAAGAAACTACCATCAGAGTGAACAGGCAACCTACAAAATGGGAGAAAAT GAM
TTTCGCAACCTACTCATCTGACAAAGGGCTAATATCCAGAATCTACAATGAACTCAAAC 26
AAATTTACAAAAAAAAAAAAAA

FIG. 22B



GAM26 GAM24

FIG. 22C



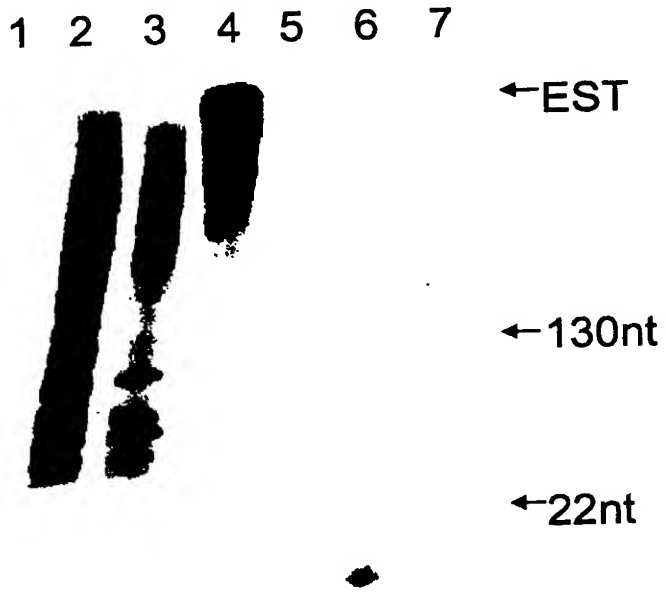
GAM26

FIG. 23A

dbEST Id.1388749 (Image1020185) Sequence:

ACTCCTATCAACAGTGTAAAAGCATTCCTGTTTCTCCATAATCTTGCCAGCATCTTTT
CATTTTTTTGAATTATAGCCATTCTGACTGTTGTGAGATGGTGTCTCATTGTGGTTTT
GATTTGCATTTCTCAGATGATCAGTGATGTTGAAGTTTTTTTGTTTGTTGGCTGCATG
TATGCCTTCTTTTGAAAAGTGTCTGTTTGTGTCCTTTGACCACTTTCTAATGGGGTTG
AGTTTTTTTTTCTTGTAAATTTGTTTAAGTTCCTTGTAGATGCTGGATATTAGACCTT
TGTCAGATGGATAGAGTGCAAAAATTTTCTCCCATTCTGTAGGTTGTCGGTTTACTCT
GTTGATAGGTTCTTAATGCTGTGCAGAAGCTCTTTAGTTTAATTAGATCCCATTTGTC
AATTTTGGCTTTTGTTGCAATTGCTTTTGGCATCTTCGTCATGAAATCTTTGCCCTTG
CCTGTGTCCTGAATGGCATTGCCTAGGTTTTCTTCCAGGATTTTTATAGTTTTGGGTT
GTAGATTTAAGTCTTTAATCCATCTTGAGTTAACTTTTGTATATGGGTTAAGGAAGGG
GCCCGTTTCAATTTGCTGCAAATGGCTAGCCAGTTCTCCCAGCACCATTTATTAAATA
GGGAATCTTTTCCCCATTGCTTCCTTTTGTCAGGTTTGTCAAAGATCACATGGTTGTA
GGTGTGTGGTCTTATTTCTGGGTTCTCTATTCTGTTCCATTGGGCTATGGGCCGGTTC
TGTACCACCACTATGCTGTTTTGGGTACCATAGTCTTGTAGAATGTTTGAAGCTGGGT
AGCATGATGCCTCTAGCTTTGCTCTTCTTGCTAAGAAATGTCTTGGCTATTTGGGCTC
TTTTTTGGTTCCATATGAATTTTAAAATAGCTTTTTCTAGGTCTGTAAAGAATGTGAA
TAGTAGTTTAATGGGCCTAGCATTTAATTTACAGATTGCCTTGGGCAGTGTGGTCATT
TTCACGATATTGATCCTTCCTGTCTGTGAGCATATGTTT**TTCCATTTGTTTGTGTCAT**GAM
CTCTGATTTCTTTGAATAATGGTTTATAGTTATCCTTGAAAAGGTCCTTCACTTTTCT 27
TGTTAGCTGTATTCCTAGATATTATACTCTTCTTGTGGCAATTGTGAATGGGAGTTAA
TTCATGAGTTTTCTCTCGGCTTGCCTGTTGTTGGTGTATAGGAATGCTAGTGACTTTT
GCACATTGATTTTGTATCCTGAGACTTTGTTGAAGTTGCTTATCAGCTAAGAAGTTTT
TGAGCTGAGATGATGGAGTTTTCTAGATATAGGATCATATCATCTGCAAACAAAGATA
GTTTGACTTCCTGTCTTCCTATTTGAATAGCTTTTCTTTCTTTCTCTTGCCTGATTGC
CTTGGTGAGAATTTCTAATACTGTGTTGAATAGGAGTGGTGAGCTCGTGCCAA

FIG. 23B



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